The results are shown in Figs. 1 and 2 wherein:

A = The product of Exampl 5

B = The product of Example 2

C = The product of Example 4

D = The product of Example 3.

IN THE CLAIMS:

Please cancel claims 2 and 9, amend claims 1, 3-8, 10-25, and 28-30, and add new claims 31-42 as follows:

1. (ONCE AMENDED) A multiparticulate bisoprolol formulation for once-daily oral administration, said formulation comprising at least two particles comprising a core of bisoprolol or a pharmaceutically acceptable salt thereof, and a polymeric coating, wherein following administration said formulation produces a bisoprolol plasma concentration of not more than about 1 ng/ml for at least about three hours, and thereafter provides a sustained release of bisoprolol that produces a therapeutic plasma concentration not later than about 12 hours following administration, and wherein said formulation maintains a therapeutic plasma concentration of bisoprolol for the remainder of a twenty-four hour period measured from administration.

2. (CANCELED)

3. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, comprising a pharmaceutically acceptable salt of bisoprolol.

4. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 3, wher in the salt is bisoprolol hemifumarate.

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5. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, which, when measured in a U.S. Pharmacopoeia 2 Apparatus (Paddles) in phosphate buffer at pH 6.8 at 37°C and 50 rpm, exhibits a dissolution profile substantially corresponding to the following:

(a) from 0% to 10% of the total bisoprolol is measured after 2 hours in said apparatus;

(b) from 0% to 50% of the total bisoprolol is measured after 4 hours in said apparatus; and

(c) greater than 50% of the total bisoprolol is measured after 10 hours in said apparatus.

6. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, which, when measured in a U.S. Pharmacopoeia 1 Apparatus (Baskets) at 37°C and 50 rpm in 0.01 N HCl for the first 2 hours followed by transfer to phosphate buffer at pH 6.8 for the remainder of the measuring period, exhibits a dissolution profil substantially corresponding to the following:

(a) from 0% to 10% of the total bisoprolol is measured after 2 hours in said apparatus;

(b) less than 50% of the total bisoprolol is measured after 4 hours in said apparatus; and

(c) greater than 20% of the total bisoprolol is measured after 10 hours in said apparatus.

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7. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the at least two particles comprise a sealant or barrier layer between the core and the polymeric coating.

8. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 7, wherein the sealant or barrier layer comprises at least one of hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl ethylcellulose or xanthan gum.

9. (CANCELED)

10. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of low permeability and wherein said at least one polymer that forms an insoluble film of low permeability comprises from about 80 to about 100 percent of the polymers in said coating.

11. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insoluble film of high permeability and wherein said at least one polymer that forms an insoluble film of high permeability comprises from about 0 to about 20 percent of the polymers in said coating.

12. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises a methacrylic acid co-polymer.

13. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 10, wherein the polymeric coating comprises an ammonio methacrylate co-polymer.

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14. (TWICE AMENDED) The multiparticulat bisoprolol formulation according to claim 10, wherein the polymeric coating comprises a mixture of methacrylate co-polymers and ammonio methacrylate co-polymers.

15. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one soluble excipient.

16. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is chosen from soluble polymers, surfactants, alkali metal salts, organic acids, sugars, and sugar alcohols.

17. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is chosen from polyvinyl pyrrolidone, polyethylene glycol, and mannitol.

18. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 15, wherein the soluble excipient is present in an amount of from 1% to 10% by weight, based on the total dry weight of polymer in the polymeric coating.

19. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises one or more auxiliary agents chosen from fillers, plasticizers, and anti-foaming agents.

20. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating produce a weight gain of from about 10% to 100% to the core.

21. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 20, wh rein th polymeric coating produce a weight gain of from about 25% to 70% to th core.

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22. (TWICE AMENDED) The multiparticulate bisoprolol formulation according to claim 1, wherein a sealant or barrier is applied to the polymeric coating.

23. (ONCE AMENDED) The multiparticulate bisoprolol formulation according claim 22, wherein the sealant or barrier comprises at least one of hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxypropyl ethylcellulose, or xanthan gum.

24. (TWICE AMENDED) An oral dosage form comprising a multiparticulate bisoprolol formulation according to claim 1, which is in the form of caplets, capsules, particles for suspension, sachets, or tablets.

25. (ONCE AMENDED) The oral dosage form according to claim 24, which is in the form of tablets chosen from disintegrating tablets, fast dissolving tablets, effervescent tablets, fast melt tablets, and mini-tablets.

28. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises a methacrylic acid co-polymer.

29. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises an ammonio methacrylate co-polymer.

30. (ONCE AMENDED) The multiparticulate bisoprolol formulation according to claim 11, wherein the polymeric coating comprises a mixture of methacrylate co-polymers and ammonio methacrylate co-polymers.

31. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one polymer that dissolves in a pH-d pendent manner.

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32. (NEW) The multiparticulate bisoprolol formulation according to claim 31, wherein the formulation releases bisoprolol in a manner that is dependent on the local pH of the gastrointestinal tract.

33. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one polymer that dissolves in a pH-independent manner.

34. (NEW) The multiparticulate bisoprolol formulation according to claim 33, wherein the formulation releases bisoprolol in a manner that is independent of the local pH of the gastrointestinal tract.

35. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation provides a sustained release of bisoprolol that produces a therapeutic plasma concentration not later than about 6 hours following administration.

36. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation further comprises talc.

37. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the formulation comprises a substantially purified enantiomer of bisoprolol.

38. (NEW) The multiparticulate bisoprolol formulation according to claim 37, wherein the substantially purified enantiomer of bisoprolol is (S)-bisoprolol.

39. (NEW) The multiparticulate bisoprolol formulation according to claim 37, wherein the substantially purified enantiomer of bisoprolol is (R)-bisoprolol.

40. (NEW) The multiparticulate bisoprolol formulation according to claim 1, wherein the polymeric coating comprises at least one pharmaceutically acceptable film-forming polymer that forms an insolubl film of low permeability.

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